REMARKS

Claims 39-43 and 74-84 are pending. Claims 1-38, 42, 44-73, 75-76, 80, 82 and 84 are canceled without prejudice as relating to a non-elected invention. Claims 39-41, 43, 74, 77, 81 and 83 are currently amended. New claims 85-108 have been added. Support for new claims 85-108 is found throughout the specification. No new matter is added by this amendment.

Applicants submit that the Response to Notice of Non-Compliant Amendment filed on October 19, 2004 failed to indicate that claim 73 was cancelled. Further, in the Response to Notice of Non-Compliant Amendment filed on October 19, 2004, claims 74 through 84 were incorrectly numbered as claims 73 through 83. Included herewith is a listing of claims wherein claims 74 through 84 are numbered correctly and in accordance with the originally filed claims.

The Examiner states at page 2 of the Office action that claims 74 and 75 are withdrawn as being directed to a non-elected invention. In view of the above, claims 74 and 75 are correctly numbered herein as claims 75 and 76. Applicants acknowledge that claims 75 and 76 are withdrawn as being directed to a non-elected invention.

Claim Objections

The Examiner objects to claim 77, as being dependent upon itself. The Examiner also objects to claims 76 and 79 as being dependent on non-elected claim 75. Applicants submit that claim 77 is correctly numbered herein as claim 78, and claims 76 and 79 are correctly numbered herein as claims 77 and 80. In view of the amendments to claims 78, 77 and 80, Applicants submit that these objections are rendered moot.

Rejection of Claims 39-43, 73 and 76-83 under 35 U.S.C. §102(b) or U.S.C. §102(e)

Claims 39-43, 73 and 76-83 are rejected under 35 U.S.C. §102(b) for alleged lack of novelty in view of WO 97/15310 or WO 00/09666, for the reasons set forth in the previous Office Action mailed on December 23, 2003.

Claims 39-43, 73 and 76-83 remain rejected under 35 U.S.C. §102(e) for alleged lack of novelty in view of WO 01/39784 or WO 02/086107, for the reasons set forth in the previous Office Action mailed on December 23, 2003.

Applicants respectfully traverse the rejections.

WO 97/15310, WO 00/09666 and WO 01/39784

The previous Office Action states at page 5 that "WO '310 teaches an isolated nestin-positive human pancreatic stem cell[s] that are not a neural stem cell[s] that can differentiate to form insulin-producing cells...[t]he method of isolating said cells is substantially similar to that used by applicant (see overlapping pages 22-24 in particular). . . WO '310 does not specifically teach that these cells are GLP-1R positive cells, said cells would inherently be GLP-1R-positive cells, since the cell population taught by WO '310 is identical to that claimed in the instant application."

The present Office Action states at page 4 that "it is the Examiner position that WO '666 teaches [an] isolated nestin-positive pancreatic stem cells that are not [a] neural stem cells that can differentiate to form insulin producing cells."

The previous Office Action states at page 6 that "WO '107 teaches an isolated nestin-positive human pancreatic stem cell[s] that are not a neural stem cell[s] that can differentiate to form insulin producing cells...while WO '107 does not specifically teach that these cells are GLP-1R positive, said cells would inherently be GLP-1R positive since the cell population taught by WO '107 is identical to that claimed in the instant application".

Applicants submit that claims 73 and 76-83 are correctly renumbered herein as claims 74 and 77-84.

Applicants submit that amended claim 39 and dependent claims 40, 43, 74 and new claim 108 include the limitation of "an isolated composition comprising at least 30% nestin-positive human pancreatic or liver stem cells that are not neural stem cells." Claim 41 and dependent claims 81 and 83 include the limitation of "an isolated composition comprising at least 30% GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells."

Support for these amendment are found throughout the specification and in particular at page 16, lines 1-13 of the instant specification wherein the term "isolated" is defined as follows:

> "Isolating" a stem cell refers to the process of removing a stem cell from a tissue sample and separating away other cells which are not stem cells of the tissue. An isolated stem cell will be generally free from contamination by other cell types and will generally have the capability of propagation and differentiation to produce mature cells of the tissue from which it was isolated. However, when dealing with a collection of stem cells, *e.g.*, a culture of stem cells, it is understood that it is practically impossible to obtain a collection of stem cells which is 100% pure. Therefore, an isolated stem cell can exist in the presence of a small fraction of other cell types which do not interfere with the utilization of the stem cell for analysis or production of other, differentiated cell types. Isolated stem cells will generally be at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98%, or 99% pure. Preferably, isolated stem cells according to the invention will be at least 98% or at least 99% pure."

Claims 42, 80, 82 and 84 are canceled.

WO '310

The invention of the WO '310 application "concerns the discovery that functional islets containing insulin-producing β-cells, as well as other islet cell types, can be grown in long-term cultures from pluripotent stem cells, which give rise to islet producing stem cells, IPSCs" (see page 8, lines 27-30). The WO '310 application discloses at page 12, lines 21-23 that "IPSCs are a small population of cells derived from **ductal** epithelial cells (i.e., these cells are pancreas-derived but are not differentiated islet cells)". (Emphasis added)

The WO '310 application teaches a method of growing IPSCs at page 13 line 29 through page 14, line 25 wherein it is stated that,

> " [t]he method of the subject invention involves making suspensions of cells, including stem cells, from the pancreas of a mammal. . .The cell suspensions are prepared using standard techniques. The cell suspension is then cultured in a nutrient medium that facilitates the growth of the IPSCs, while at the same time severely compromising the sustained growth of the differentiated or mature cells other than IPSCs. . . What is required for such media is that they have little or no glucose (less than about 1 mM) and low serum (less than about 0.5%). The high

> amino acid concentrations are preferably of amino acids known to be essential for the cells of the species being cultured, and provide a carbon source for the cultured cells. In addition, at least one rudimentary lipid precursor, preferably pyruvate, is provided. These conditions are so stressful to most differentiated cell types that they do not survive. Surprisingly, however, upon extended culture of cells from pancreatic tissue without re-feeding (about 3 weeks) IPSCs do survive and after extended culture, begin to proliferate."

WO '666

The WO 00/09666 publication relates to "a population of insulin producing cells made by a process comprising contacting non-insulin producing cells with a growth factor selected from the group consisting of GLP-1 or Exendin-4 growth factors having amino acid sequences substantially homologous thereto, and fragments thereof." The WO '666 application states at page 14, lines 23 through 30 and page 15, lines 8:

> "[b]y 'non-insulin producing cells' is meant any cell that does not naturally synthesize, express, or secrete insulin constitutively or inducibly...the term 'non-insulin producing cells' as used herein **excludes beta cells**...Examples of non-insulin producing cells that can be used in the methods of the present invention include **pancreatic non-beta cells**, such as amylase producing cells, **acinar** cells, cells of **ductal** adenocarcinoma cell lines... and stem cells...[e]xamples of the present method using mammalian **pancreatic non-islet**, pancreatic amylase producing cells, pancreatic acinar cells, and stem cells are provided herein. Stem cells can include pancreatic stem cells and non-pancreatic stem cells that have been promoted to produce IDX-1, Beta 2/NeuroD, and E47...[p]ancreatic stem cells include **duct** epithelial precursor cells which give rise to both islet and acinar cells."

The only working examples in the WO 00/09666 publication that teach the use of cells are limited to the AR42J cell line (an acinar cell line) (See Examples 4 and 5). As indicated on page 1, lines 30-31, of the WO '666 publication, "acinar cells, which are present in the pancreatic **ducts**, produce exocrine enzymes." (Emphasis added)

Pancreatic islets contain three major types of cells (alpha, beta and delta cells). The largest number of cells are the beta cells which produce insulin. The alpha cells produce glucagon and the delta cells produce somatostatin. The WO '666 application does not teach alpha, beta or delta cells as a source of insulin producing cells. In fact, beta cells are specifically excluded from the definition of "non-insulin producing cells" recited in the WO '666 application. One of

skill in the art would therefore recognize that in view of the above recited definition of "non-insulin producing cells", the WO '666 application is limited to insulin producing cells that are derived from the pancreatic duct or from non-pancreas tissue.

WO '107

The WO 02/086107 publication teaches differentiation of stem cells, wherein the stem cells are preferably ES or EG cells (see page 5, lines 4-5 wherein the WO '107 publication states that "[t]he present invention is aimed at inducing the differentiation of ES cells by activation of specific genes into insulin-producing cells"; page 8, lines 25-27, " 'cultivation medium' means a suitable medium capable of supporting growth and differentiation of stem cells, preferably ES and EG cells."). The WO 02/086107 also discloses a method of differentiating ES cells into insulin-producing cells using culture conditions that favor the formation of nestin-positive cells (see Example 8, page 27 through 28) as well as a method of selecting nestin-positive cells from embryoid bodies (see page 13, lines 11-17). This publication does not teach a stem cell isolated from a pancreas.

Applicants submit that for a determination of anticipation to be proper, the prior art reference must disclose each and every limitation of the claim. *Atlas Powder Company et al. v. IRECO, Incorporated et al.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999).

None of the WO '310 application, the WO '666 application and the WO '107 application teach or suggest an isolated composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98% or 99% nestin, GLP-1R or nestin and GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells as required by the instant claims.

Applicants submit that none of the WO '310 application, the WO '666 application or the WO '107 application teach "an isolated composition comprising at least 30% nestin-positive human pancreatic or liver stem cells that are not neural stem cells" as required by claim 39 and dependent claims 40, 43 and 74 of the instant application. Applicants submit further that none of the WO '310 application, the WO '666 application or the WO '107 application teach " an isolated composition comprising at least 30%, GLP-1R-positive human pancreatic or liver stem

cells that are not neural stem cells" as required by instant claim 41 and dependent claims 81 and 83.

Applicants submit further that none of the WO '310 application, the WO '666 application or the WO '107 application teach "an isolated composition comprising at least 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98%, or 99% nestin-positive human pancreatic or liver stem cells that are not neural stem cells" as required by new claims 85 through 94. Applicants also submit that none of the WO '310 application, the WO '666 application or the WO '107 application teach " an isolated composition comprising at least 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98%, or 99%, GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells" as required by new claims 95 through 104.

Support for these claims, as well as the amendments to claim 39 and 41 is found in the definition of "isolating" presented in the instant specification at page 16, lines 1 through 13 (recited hereinabove).

Amended claims 77, 78 and 79 relate to an isolated nestin-positive, GLP-1R-positive or nestin and GLP-1R-positive human pancreatic stem cell isolated by a) removing a pancreatic **islet** from a donor; b) removing cells from the pancreatic **islet** wherein the islet comprises a plurality of cell types comprising stem cells; and c) separating the stem cells from the plurality of cells.

New claims 105 through 107 relate to an isolated nestin-positive, GLP-1R-positive or nestin-positive and GLP-1R positive cell isolated from a pancreatic **islet**.

Support for these claims is found throughout the specification and in particular in Example 1.

The instant specification teaches one embodiment of a method of isolating nestin-positive stem cells from rat pancreas, that includes a step of isolating rat islets from a pancreas. (see Example 1, p. 48, line 17). That is, the starting material is pancreatic islets. It is also stated in the instant specification at page 23, lines 25 through 27 that "[p]revious investigators have focused on ductal epithelial cells of pancreatic islets or exocrine tissue as a possible source of stem cells for the neogenesis of islet endocrine cells." In view of the above, one aspect of the

novelty of the instant application is an isolated nestin-positive stem cell isolated from a pancreatic **islet**.

None of the WO 97/15310 reference, the WO 00/09666 reference or the WO 01/39784 reference teach an isolated nestin-positive, GLP-1R-positive or nestin-positive and GLP-1R-positive cell isolated by a) removing a pancreatic **islet** from a donor; b) removing cells from the pancreatic **islet** wherein the islet comprises a plurality of cell types comprising stem cells; and c) separating the stem cells from the plurality of cells, as claimed in claims 77 through 79 of the instant application. Rather, the WO '310, WO '666 and WO '107 applications teach cells derived from pancreatic **ducts** or other non-pancreas sources.

Inherency

Applicants submit that the Examiner must provide rationale or evidence tending to show inherency to properly make a rejection under 35 U.S.C. 102 when the prior art is silent as to an inherent characteristic (MPEP §2112).

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) ...; *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. **Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient**.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (Emphasis) (MPEP §2112, citations omitted).

Applicants submit that none of the WO '310 application, the WO '666 application or the WO '107 application teach a composition that is inherently "an **isolated** composition comprising at least 30% 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98%, or 99% nestin-positive human pancreatic or liver stem cells that are not neural stem cells" as required by claims 39, 40, 43, 74 and 85 through 94. (Emphasis added)

Applicants submit that none of the WO '310 application, the WO '666 application or the WO '107 application teach a composition that is inherently "an **isolated** composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98%, or 99% GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells" as required by claims 41, 81, 83 and 95 through 104. (Emphasis added)

Applicants previously presented a Declaration under 37 C.F.R. § 1.132 by Dr. Habener (presented with the response to Office Action filed on June 21, 2004; copy provided herein), which presents at page 5, line 2 through page 6 line 10, estimates for the number and percent of nestin-positive cells in the pancreas, pancreatic islets and pancreatic ducts. As stated in the declaration, "the percentage of nestin-positive cells in the pancreas is in the range of 0.2 to 5%" (see page 6). Further, "[t]he islets make up approximately 2% of the total pancreas tissue...the contribution of nestin positive cells from the islets is 2% of 6.2%, or 0.124%." (see page 6). Dr. Habener also states at page 5 that "the contribution of nestin-positive cells from the non-islet cells of the pancreas is ...4.25%." As stated at page 5, line 11 of the declaration, "only 2-3% of the entire pancreas are islets and ducts." Therefore, one of skill in the art would accept that if the islets make up approximately 2% of the total pancreas, the ducts make up approximately 1% of the pancreas. One of skill in the art would also accept that the contribution of nestin positive cells from the non-islet cells of the pancreas (ductal cells) is 1% of 4.25% or .04%.

As stated above, none of the WO '310 application, the WO '666 application and the WO '107 application teach or suggest an isolated composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98% or 99% nestin, GLP-1R or nestin and GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells as required by the instant claims.

In view of the above analysis, Applicants respectfully submit that the Examiner is incorrect in his statement at page 3 that the "[d]eclaration by Dr. Habener...stated that the number of nestin-positive cells in the pancreas is in the range of .02 to 5%...[h]owever, said numbers are irrelevant since WO '310 teaches that the pancreatic stem cells were isolated from non-islet cells of the pancreas." As discussed above, the declaration of Dr. Habener discloses

that the percentage of nestin-positive cells derived from non-islet cells of the pancreas is on the order of 0.4%.

Further in view of the above, one of skill in the art would not accept that "an isolated composition comprising at least 30% nestin-positive human pancreatic or liver stem cells that are not neural cells" or "an isolated composition comprising at least 30% GLP-1R positive human pancreatic or liver stem cells that are not neural stem cell" as required by claims 39-41, 43, 74, 81 and 83 of the instant application would inherently be identical to any one of the suspension of stem cells disclosed in the WO '310 application, the population of insulin-producing cells disclosed in the WO '666 application and the insulin producing cells of the WO '107 application.

Given the small percentage of nestin-positive and GLP-1R positive cells in the pancreas (either in the islets or the ducts), one of skill in the art would not accept that any one of the WO '310 application, the WO '666 application or the WO '107 application teach "an **isolated** composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98% or 99% nestin, GLP-1R or nestin and GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells" as required by the instant claims and according to the definition of "isolated" presented in the instant application (recited hereinabove). (Emphasis added)

An "**isolated** composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98% or 99% nestin, GLP-1R or nestin and GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells" or an "**isolated** nestin or GLP-1R positive human pancreatic or liver stem cell that is not a neural stem cell" can be produced by any one of the following methods.

a) The instant specification teaches one embodiment of a method of isolating a composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98% or 99% nestin, GLP-1R or nestin and GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells in Example 1 (see page 48, line 15 through page 49, line 27) wherein the instant specification states:

"Rat islets were isolated from the pancreata of 2-3 month old Sprague-Dawley rats using the collagenase digestion method described by Lacy and Kostianovsky. Human islets were provided by the Diabetes Research Institute, Miami, FL using collagenase digestion. The islets were cultured for 96 hrs at 37°C in 12-well plates (Falcon 3043 plates, Becton Dickinson, Lincoln Park, NJ) that had been coated with concanavalin A. The culture medium was RPMI 1640 supplemented with 10% fetal bovine serum, 1mM sodium pyruvate, 10mM HEPES buffer, 100 μg/ml streptomycin, 100 units/ml penicillin, 0.25 μg/ml amphotericin B (GIBCO BRL, Life Science Technology, Gaithersburg, MD), and 71.5 mM β-mercaptoethanol (Sigma, St. Louis, MO).

After 96 hrs, fibroblasts and other non-islet cells had adhered to the surface of concanavalin A coated wells and the islets remained floating (did not adhere to the surface). At this time, the media containing the islets were removed, centrifuged down, and the purged islets replated in 12-well plates without a coating of concanavalin A. The islets were then cultured in the above RPMI 1640 medium supplemented with 20 ng/ml of basic fibroblast growth factor-2 and 20 ng/ml of epidermal growth factor.

The islets adhered to the surface of the plates, and cells grew out and away from the islets in a monolayer. **These cells that form a monolayer were nestin-positive by immunostaining with a rabbit anti-rat nestin antiserum** developed by Dr. Mario Vallejo at the Massachusetts General Hospital. Other nestin antibodies may be used, for example the R.401 antibody described hereinabove, or the MAB533 antibody. A monoclonal antibody specific for rat embryo spinal cord nestin, MAB353, ATCC No. 1023889; is described in Journal of Neuroscience 1996; 16:1901-100; and also available from Chemicon International, Single Oak Dr., Temecula, CA 92590 USA. **After two weeks of culture, several (3-5) of the nestin-positive monolayer cells were removed by picking with a capillary tube (cylinder cloning) and were replated** on the 12-well plates (not coated with concanavalin A) and cultured in the RPMI 1640 medium further supplemented with bFGF-2 and EGF. The cells propagated at a rapid rate and reached confluence after six days of culture. After 12 days of culture, the cell monolayer formed waves in which they begin to pile up in a co-linear manner. On day 15 of culture, the cell waves began to condense, migrate into spheroid bodies and by day 17 the surface of the wells contained these spheroid bodies (ca. 100 μm in diameter), empty spaces, and a few areas of remaining monolayer cells. Several of these monolayer cells were re-picked and re-cloned and the process described above occurred again in precisely the same temporal sequence." (Emphasis added)

b) Attached to Applicant's response to Office Action filed on June 21, 2005 was a post-filing publication from the inventor's laboratory (Abraham et al., *2002, Endocrinology*, 143:3152, Exhibit A) wherein nestin-positive islet-derived progenitor cells are identified as

follows: "islets were washed and cultured in RPMI 1640 medium containing serum, 11.1 mM glucose, antibiotics, sodium pyruvate, β-mercaptoethanol, and growth factors. Within several days, nestin-positive progenitor cells grew out from islets. These cells were cloned and expanded in medium containing 20 ng/ml each of bFGF and EGF." This publication describes an additional embodiment of a method of isolating a "composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98% or 99%, nestin, GLP-1R or nestin and GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells".

c) The copy of the Rule 1.132 declaration of Dr. Habener (filed on June 21, 2004) states that nestin-positive cells can be isolated by digesting islets with trypsin to prepare single cell suspensions of human pancreatic islet preparations and growing the resulting cells in an appropriate medium, for example RPMI 1640 (11 mmol/l glucose) with 10 mmol/l Hepes buffer, 1 mmol/l sodium pyruvate, 10% fetal bovine serum, 25 ng/ml EGF, 20 ng/ml bFGF and 1X penicillin/streptomycin. The resulting expansion cultures of progenitor cells contain two major populations of cells that are phenotypically distinct cell types; those that express nestin and vimentin and those that express epithelial markers cytokeratin 19 and E-cadherin, as detected by immunofluorescence.

The two major populations of cells are easily separated based on differences in their morphologies. The nestin/vimentin positive spindle shaped fibroblast-like cells are markedly different from that of the E-cadherin/CK19 positive, flat, cuboidal epithelial-like cells that are in patches. Under regular or phase contrast light microscopy, using low power, nestin/vimentin positive cells that are clearly separated from the E-cadherin/CK19 cells which grow in distinct patches, are selected.

d) One skilled in the art will appreciate that a variety of separation strategies based on immunophenotyping methodologies such as surface coated antibody panning, fluorescent antibody tagging for physical isolation, flow cytometric sorting, immunomagnetic bead and particle selection and counterselection will be useful in carrying out the present invention. As shown herein, a number of selection criteria can be employed to allow the isolation of distinct populations of nestin+/vimentin+/cytokeratin 19-/E-cadhedrin- cells. It is also appreciated by

one skilled in the art that other markers known in the field, using similar separation strategies, can be employed to isolate distinct populations of nestin+ cells.

Support for such methods is also disclosed in the instant specification which states at page 24, lines 21-25 that "[s]tem cells according to the invention can be identified by their expression of nestin or GLP-1R, or co-expression of nestin and GLP-1R by, for example, FACS, immunocytochemical staining, RT-PCR, Southern, Northern and Western blot analysis, and other such techniques of cellular identification as known to one skilled in the art." The instant specification characterizes the markers present on the stem cells of the invention (see page 30) and also discloses antibodies to stem cell markers including nestin, GLP-1R, vimentin and cytokeratin-19 (see page 25).

In view of all of the above, one of skill in the art would not accept that it is necessarily probable or possible that the suspension of stem cells of the WO '310 application or the insulin-producing cells of either the WO '666 or WO '107 application are inherently "an **isolated** composition comprising at least 30% nestin-positive human pancreatic or liver stem cells that are not neural stem cells" or "an **isolated** composition comprising at least 30% GLP-1R-positive human pancreatic or liver stem cels that are not neural stem cells" as required by claims 39-41, 43, 74, 81 and 83 of the instant application.

One of skill in the art would also not accept that it is necessarily probable or possible that the suspension of stem cells of the WO '310 application or the insulin-producing cells of the WO '666 application or the WO '107 application are inherently "an isolated composition comprising at least 30% 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98%, or 99% nestin-positive human pancreatic or liver stem cells that are not neural stem cells" as required by claims 39, 40, 43, and 85 through 94; or "an isolated composition comprising at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95%, 98%, or 99% GLP-1R-positive human pancreatic or liver stem cells that are not neural stem cells" as required by claims 41, 81, 83 and 95 through 104.

Applicants respectfully submit that the Examiner has not provided extrinsic evidence that makes clear that "the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill".

In view of all of the above, Applicants submit that claims 39-41, 43, 74, 78, 79, 81, 83, and new claims 85 through 108 are novel in view of the WO 97/15310, WO 00/009666 and WO 02/086107 applications.

WO 01/39784

In response to the Examiner's statement at page 5 of the Office Action that "there was no attached statement of common ownership of the WO '784 and the instant application", Applicants are submitting said statement.

35 U.S.C. 103(c) states that "[s]ubject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."

The MPEP states in section 706.02(l)(1) at page 700-50, "[e]ffective November 29, 1999, subject matter which was prior art under former 35 U.S.C. 103 via 35 U.S.C. 102(e) is now disqualified as prior art against the claimed invention if that subject matter and the claimed invention 'were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person'".

As indicated in the attached statement, the inventors of the WO 01/39784 reference and the inventors of the instant application were, at the time each of the inventions were made, subject to an obligation of assignment to the same person.

In view of the common ownership of the WO 01/39784 reference and the instant application, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 39-43, 74 and 77-84 under 35 U.S.C. §102(e).

In view of all of the above, Applicants submit that claims 39-41, 43, 74, 78, 79, 81, 83, and new claims 85 through 108 are novel in view of the WO 97/15310, WO 00/009666, WO 02/086107 and WO 01/39784 applications. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §102(a) and §102(e)rejection.

CONCLUSION

Applicants submit that in view of all of the above, all claims are allowable as written and respectfully request early favorable action by the Examiner.

Respectfully submitted,

Date: December 23, 2005

Elizabeth M S Reg #45,123

Name: Kathleen M. Williams
Registration No.: 34,380
Customer No.: 29933
Edwards Angell Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel: 617-239-0100